

Drug Utilization Pattern Study of Magnesium Sulphate In Pregnant Patients with Preeclampsia at Mohammad Hoesin Hospital, Palembang

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Abstract

Preeclampsia is a hypertensive disorder of pregnancy characterized by systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two measurements taken at least 4 hours apart after 20 weeks of gestation, accompanied by new-onset proteinuria. Preeclampsia with severe features may progress to eclampsia. Magnesium sulphate is recommended for seizure prophylaxis because of its effectiveness and relatively low risk of serious neonatal adverse effects. This study aimed to evaluate the appropriateness of magnesium sulphate prescribing in pregnant women with preeclampsia at Mohammad Hoesin Hospital Palembang based on predefined prescribing indicators. This descriptive drug utilization study was conducted from August to September 2024 using total sampling of medical records that met the inclusion criteria, resulting in 45 samples. Data were analyzed using SPSS version 27.0 for MacOS and presented as frequency distributions. The prevalence of preeclampsia was 77.46%. All patients had preeclampsia with severe features (100%); most were housewives (68.9%), multiparous (55.5%), multigravida (80%), and had a gestational age ≥ 34 weeks (71.1%). Magnesium sulphate use was appropriate regarding indication (100%), dosage regimen (100%), duration of administration (100%), and absence of contraindications (100%). Eighteen patients (40%) received concomitant nifedipine, while 27 patients (60%) had no identified potential drug interactions. Overall, magnesium sulphate uses in pregnant women with preeclampsia at Mohammad Hoesin Hospital Palembang met the evaluated rational drug use criteria.

Keywords: Magnesium Sulphate, Preeclampsia, Drug Utilization Study

1. Introduction

Preeclampsia is new-onset hypertension occurring after 20 weeks of gestation defined by systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg on two occasions at least 4 hours apart accompanied by proteinuria with ≥ 300 mg/day or protein/creatinine ratio 0.3 mg/dL or urine dipstick test result +2 and organ dysfunction. Preeclampsia can be accompanied by organ dysfunction even without proteinuria, such as renal insufficiency, liver failure, hematological disorders, pulmonary edema, neurological disorders and uterine-placental dysfunction.¹⁻³

³ Preeclampsia is associated with 2-8% of pregnancy complications worldwide, causing

more than 70.000 maternal deaths and 500.000 fetal deaths annually.^{1,4} Preeclampsia cases in developing countries are more prevalent than in developed countries. Preeclampsia prevalence in developing countries ranges from 1.8-18%, while in developed countries it ranges from 1.3-6%.^{5,6}

The history of preeclampsia in previous pregnancies, chronic hypertension, pregestational diabetes mellitus, multifetal pregnancy, and obesity are the main risk factors for preeclampsia.⁴ The pathogenesis of preeclampsia is associated with placental dysfunction, maternal systemic inflammatory responses involving endothelial activation and coagulation, imbalance in the role of angiogenic factors and increase in

antiangiogenic factors.⁵ The diagnostic classification of preeclampsia can be divided into preeclampsia without severe features and preeclampsia with severe features.¹ Preeclampsia can worsen rapidly, presenting severe features that may lead to serious complications, such as eclampsia (seizures) and HELLP syndrome (Hemolysis, Elevated Liver Enzymes and Low Platelet Count). Eclampsia is the most severe complication of preeclampsia, characterized by new-onset tonic-clonic, focal or multifocal seizures without other underlying causes, such as epilepsy, intracranial hemorrhage, cerebral artery infarction, or drug-induced seizures.^{1,7,8}

One of the management options in preeclampsia is the administration of magnesium sulphate to prevent and treat seizures (eclampsia).^{6,9} Magnesium sulphate acts as a calcium antagonist, promoting vasodilation by relaxing smooth muscles in peripheral and uterine blood vessels, so that it functions as both an antihypertensive and a tocolytic agent. Additionally, this drug inhibits N-Methyl-D-Aspartate (NMDA) receptors in the brain, specifically glutamate receptors, where excessive stimulation due to asphyxia may mediate the occurrence of seizures.^{6,10} The effectiveness of magnesium sulphate in reducing and preventing eclampsia is considered superior to diazepam, phenytoin and nimodipine.¹ Magnesium sulphate is administered with an initial dose of 4 grams intravenously over 20 minutes or if intravenous access is difficult, it can be given intramuscularly with an initial dose of 10 grams. Subsequently, a maintenance dose of 6 grams is given over 6 hours.¹¹

Drug utilization research is an important component of pharmacoepidemiology that evaluates how medicines are prescribed and used in clinical practice to promote rational and appropriate medicine use. Such evaluations may assess indication, dosage regimen, route of administration, duration of

therapy, potential drug interactions, contraindications, and other relevant clinical factors.¹² The Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) system is an internationally recognized method for measuring and comparing drug utilization. However, drug utilization evaluation may also focus on the appropriateness of prescribing based on clinical criteria and treatment guidelines. Therefore, evaluating MgSO₄ prescribing using predefined clinical indicators is important to assess the appropriateness and safety of its use in patients with preeclampsia.^{12,13}

Although magnesium sulphate is widely recommended for seizure prophylaxis in preeclampsia with severe features, inappropriate prescribing may increase the risk of toxicity that leads to maternal morbidity and mortality. Evaluation of prescribing practices should therefore consider specific prescribing indicators rather than assuming that administration is entirely rational based on the diagnosis alone.^{1,8} In the present study, the evaluation was focused on selected indicators that could be reliably assessed from retrospective medical records, namely indication, dosage regimen, duration of administration, potential drug interactions, and contraindications. The objective of this study was to evaluate the appropriateness of magnesium sulphate prescribing in pregnant women with preeclampsia based on predefined prescribing indicators at Mohammad Hoesin Hospital Palembang during the period of 1 July 2022 to 30 June 2023.

2. Methods

This study was a retrospective descriptive drug utilization study based on medical record data of patients diagnosed with preeclampsia who received magnesium sulphate. The study was conducted at the

Department of Obstetrics and Gynecology, Mohammad Hoesin Hospital Palembang, Indonesia. Medical records of pregnant women with hypertension in pregnancy hospitalized between 1st July 2022-30th June 2023 were reviewed. Patients were excluded if they had preeclampsia complicated by eclampsia. Data collection was conducted from August to September 2024.

A total sampling technique was used. All medical records that met the predefined inclusion and exclusion criteria were included in the study. The variables evaluated in this study included patient characteristics and the appropriateness of magnesium sulphate use. The appropriateness of therapy was assessed based on indication, dosage regimen, duration of administration, drug interactions, and contraindications. The appropriateness of magnesium sulphate use was assessed based on predefined prescribing criteria derived from the clinical guidelines and predefined operational criteria based on the clinical guideline applicable at Mohammad Hoesin Hospital during the study period to provide an objective and standardized assessment of magnesium sulphate utilization.

Appropriate indication was defined as magnesium sulphate administration for seizure prophylaxis in pregnant women diagnosed with preeclampsia and predefined severe features. Appropriate dosage regimen was defined as administration of a 4–6 g intravenous loading dose over 15–20 minutes followed by a maintenance dose of 1–2 g/hour.^{1,7,8} Appropriate duration was defined as administration for ≥ 24 hours.¹⁰ The absence of contraindications was defined as no documented myasthenia gravis, hypocalcaemia, moderate-to-severe renal failure, cardiac ischemia, heart block,

myocarditis, or hypersensitivity to magnesium sulphate.¹ Potential drug interactions were assessed based on concomitant medications documented in the medical records. Each indicator was analyzed descriptively as frequency and percentage. Ethical approval was obtained from the Health Research Ethics Committee, Faculty of Medicine, Universitas Sriwijaya (protocol number: 167-2024).

3. Results

The prevalence of preeclampsia among hospitalized pregnant women with hypertensive disorders of pregnancy at Mohammad Hoesin Hospital from July 1, 2022, to June 30, 2023, was 77.46%. Out of these 134 patients with preeclampsia, 89 were excluded due to incomplete medical record data and complications of eclampsia, resulting in 45 patients who met the eligibility criteria and were included in the study.

All patients were diagnosed with preeclampsia with severe features meeting the diagnostic criteria, which included blood pressure $\geq 160/100$ mmHg, platelet count $<100,000/\mu\text{L}$ and new-onset headache unresponsive to medication. The demographic characteristics of the study population revealed that the majority of pregnant women with preeclampsia receiving MgSO_4 were aged between 20 and 35 years (60%). The predominant occupational category was housewives (68.9%). Multiparous women constituted the largest parity group (55.5%), while multigravida patients represented the majority based on gravida classification (80%). The majority of gestational age classifications found were gestational age ≥ 34 weeks (28.9%).

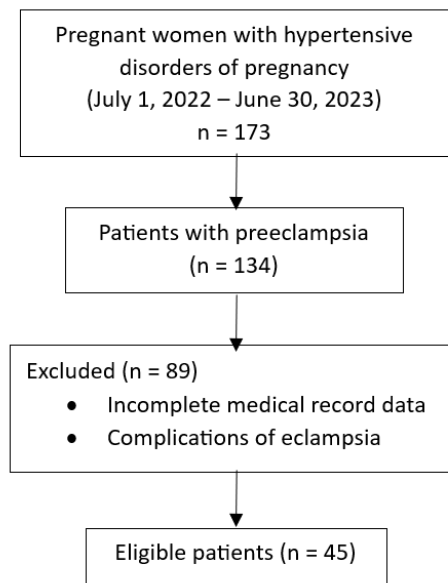


Figure 1. Selection of Study Participants Based on Eligibility Criteria

Table 1. Prevalence of Preeclampsia Among Pregnant Women with Hypertensive Disorders of Pregnancy

Prevalence of preeclampsia patients	Total (n)	Percentage (%)
Preeclampsia (+)	134	77,46
Preeclampsia (-)	39	22,54
Total	173	100

*Table 2. Characteristics of Pregnant Women with Preeclampsia Receiving Magnesium Sulphate

Variables	Total (n)	Percentage (%)
Classification of preeclampsia		
Preeclampsia without severe features	0	0
Preeclampsia with severe features	45	100
Age		
< 20 years	1	2,2
20 – 35 years	27	60
> 35 years	17	37,8
Occupation		
Housewife	31	68,9
Civil Servants	1	2,2
Self-employed	0	0
Private employee	7	15,6
Non-Permanent employee	1	2,2
Others	5	11,1
Parity		
Nullipara	12	26,7
Primipara	8	17,8
Multipara	25	55,5
Gravida		
Primigravida	9	20
Multigravida	36	80
Gestational age		
< 34 weeks	13	28,9
≥ 34 weeks	32	71,1

All patients received MgSO_4 with an appropriate indication. The administration of MgSO_4 was in accordance with clinical guidelines being prescribed for patients diagnosed with preeclampsia with severe features who met the diagnostic criteria. The most common use of MgSO_4 was an initial dose regimen of 4–6 grams administered slowly intravenously over 15–20 minutes followed by a maintenance dose of 1–2 grams per hour intravenously as observed in all patients. Based on the duration category of magnesium sulphate administration, all patients in this study received the treatment for ≥ 24 hours.

Drug interactions refer to reactions that occur when magnesium sulphate is used combination with other drugs. In this study, the majority of cases showed no drug interaction (60%). A potential pharmacodynamic interaction requiring clinical monitoring was identified in 18 patients (40.0%) who received magnesium sulphate concomitantly with nifedipine. The concomitant use of magnesium sulphate and nifedipine was not classified as inappropriate prescribing; rather, it was considered a potential interaction that warrants clinical monitoring.

Table 3. Frequency distribution of drug utilization pattern study of MgSO_4 in pregnant women with preeclampsia at Mohammad Hoesin Hospital period of 1st July 2022 – 30th June 2023

Drug Utilization Pattern Study	Total (n)	Percentage (%)
Indications for administration		
Right indication	45	100
Inappropriate indication	0	0
Dosage regimen		
Initial dose 4–6 grams slowly IV over 15–20 minutes followed by a maintenance dose of 1–2 grams/hour IV	45	100
Initial dose of 4 grams IV and 10 grams IM (5 grams each in the right and left buttocks) followed by a maintenance dose of 5 grams IM every 4 hours	0	0
Duration of administration		
< 24 hours	0	0
≥ 24 hours	45	100
Drug interactions		
Synergistic	18	40
No interaction	27	60
Appropriate contraindications		
Appropriate contraindications	0	0
Myasthenia gravis		
Hypocalcaemia		
Moderate to severe renal failure		
Heart ischemia		
Heart block		
Myocarditis		
History of hypersensitivity reaction MgSO_4		
Inappropriate contraindications	0	0
No contraindications	45	100
Total	45	100

Table 4. Drug utilization pattern study of MgSO₄ in pregnant women with preeclampsia at Mohammad Hoesin Hospital period of 1st July 2022 – 30th June 2023

Variables	Appropriate		Total
	Yes (%)	No (%)	
Indications for administration	100	0	100
Dosage regimen	100	0	100
Duration of administration	100	0	100
Drug interactions	Synergistic : 40 None : 60	Antagonist : 0 Potentiation : 0	100
Contraindication	100	0	100

Contraindications in this study refer to special patient conditions for which magnesium sulphate should not be administered, as it may worsen the patient's condition. Among the 45 patients, none had contraindications to the use of MgSO₄. According to this study, the administration of MgSO₄ in pregnant women with preeclampsia was found to be appropriate in terms of indication, dosage regimen, duration of administration, drug interactions, and no contraindications.

4. Discussion

This study identified a prevalence of preeclampsia of 77.46% among hypertension in pregnancy. This result aligns with the findings of research by Rahis et al. (2020) that the prevalence of preeclampsia was 72%.¹⁴ The indication for MgSO₄ administration in this study was appropriate in all patients based on the predefined criteria. MgSO₄ was administered as seizure prophylaxis for patients with preeclampsia with severe features meeting one or more diagnostic criteria: systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg in two occasions at least 4 hours apart, thrombocytopenia, renal insufficiency, impaired liver function, pulmonary edema, new-onset headache unresponsive to medication and not accounted for by alternative diagnoses, and visual symptoms.^{1,16} This finding reflects the study population, as all included patients had preeclampsia with severe features, and

therefore indicates consistency between the documented indications and predefined criteria rather than universal appropriateness of MgSO₄ use in all patients with preeclampsia. These findings are consistent with research by Tamaledu et al. (2023) also reported that 81.8% of preeclampsia cases involved severe features, while only 18.2% were without severe features.¹⁵ The administration of MgSO₄ in preeclampsia can reduce the risk of eclampsia by 58% compared to placebo.¹⁶ The 100% appropriateness observed in this study may therefore be explained primarily by the predefined inclusion criteria, which restricted the analysis to patients with severe preeclampsia who had an established indication for MgSO₄. In addition, patients with eclampsia were excluded, further narrowing the study population to patients receiving MgSO₄ for seizure prophylaxis rather than treatment of established seizures. However, maternal and neonatal outcomes following administration were not assessed in this study.

The dosage regimen of MgSO₄ in this study was entirely consistent with the predefined dosage criteria, with an initial dose regimen of 4 grams intravenously over 15-20 minutes followed by a maintenance dose of 1 gram/hour intravenously. This regimen aligns with the findings of Akbar et al. (2020) that every preeclampsia patient with severe symptoms was given MgSO₄ at this dose regimen.¹⁶ In addition, the study of Akhtar et al. (2023) found that this dose regimen was mostly used in patients with severe

preeclampsia and eclampsia, as many as 113 patients (43.5%) out of a total of 260 patients.¹⁷ An initial dose of 4–6 grams IV corresponds to a rapid doubling of the baseline concentration of MgSO_4 within ½ hour of starting the injection. A maintenance dose of 1 gram/hour will result in an average concentration of between 1–2 mmol/l over the period of administration.¹⁸ Although intravenous magnesium sulphate requires monitoring because of the potential for toxicity, this study did not evaluate serum magnesium concentrations or systematic toxicity monitoring.

In this study, all patients received the intravenous regimen, consistent with reports from other tertiary-care settings, although administration practices vary across countries and institutions. In Thailand, Charoenvidhya et al. reported intravenous MgSO_4 administration using a 5-g loading dose followed by continuous maintenance at 1 or 2 g/hour for 24 hours postpartum.¹⁹ In India, intravenous regimens have also been reported, although some centers use intravenous and intramuscular regimens comparatively.²⁰ These findings indicate that intravenous administration is an established approach in different clinical settings, while the 100% intravenous use observed in the present study may reflect local clinical practice and institutional protocols rather than a universal prescribing pattern.

Magnesium sulphate in the study was administered for 24 hours, in All patients, which was consistent with the predefined duration criterion. This aligns with the research of Akbar et al. (2020) which found that the majority of the duration of MgSO_4 administration was ≥ 24 hours involving 25 patients out of 43 patients.¹⁶ The 2020 ACOG practice bulletin and the 2016 POGI Preeclampsia Management PNPk similarly recommend that MgSO_4 infusion be continued for 24 hours postpartum.^{1,6}

Drug interactions identified in this study included 60% with no potential interaction and 40% with a potential synergistic interaction. No interaction is defined as the absence of an interaction that alters the effects of the drugs. The synergistic interaction occurred between magnesium sulphate and nifedipine. This drug combination was also reported in a study by Putri et al. (2020) as the most common drug combination used in preeclampsia patients with severe symptoms at 93.75%.²¹ Similarly, research by Julaeha et al. (2021) found that the combination of nifedipine and magnesium sulphate was used in 78 patients (79%).²² While magnesium sulphate effectively controls seizures, it is less effective in managing blood pressure. Therefore, antihypertensives are often co-administered to preeclampsia patients with severe features. Nifedipine is commonly used for blood pressure control in patients with severe preeclampsia and may be co-administered with MgSO_4 when clinically indicated. Nifedipine promotes vasodilation through calcium-channel blockade, while magnesium sulphate contributes to vascular smooth muscle relaxation. The combination of magnesium sulphate and nifedipine represents a potential pharmacodynamic interaction because both agents may contribute to vasodilation and blood pressure reduction. Therefore, monitoring of blood pressure and neuromuscular status remains important during treatment.^{23,24} Research by Putri et al. (2020) on the combination of MgSO_4 and nifedipine found no adverse effects, but monitoring is still carried out. When administering anticonvulsants, it is also important to prepare calcium gluconate as an antidote.²¹

This study found that none of the 45 patients (100%) had a documented contraindication to magnesium sulphate. The absence of documented contraindications

suggests that magnesium sulphate prescribing was consistent with the predefined safety criteria in the available medical records. However, because this study was retrospective, the absence of documentation cannot confirm that every contraindication was systematically assessed in every patient.

MgSO₄ can exacerbate neuromuscular weakness through a competitive mechanism at the neuromuscular junction in patients with myasthenia gravis, potentially causing a myasthenic crisis or transient quadriplegia.²⁵ Hypocalcemia may worsen when MgSO₄ is given because according to Farahani et al.(2022) giving a 24-hour intravenously infusion of MgSO₄ led to hypocalcemia in 50% of patients.²⁶ In patients with cardiac dysfunction, such as ischemia or myocarditis, the vasodilatory effects of magnesium sulphate may impair cardiac perfusion potentially leading to complications like myocardial infarction or arrhythmias.^{27,28} Additionally, patients with impaired renal function are at increased risk of hypermagnesemia during MgSO₄ therapy because reduced renal excretion may lead to magnesium accumulation.²⁹ These considerations highlight the importance of clinical assessment and monitoring when magnesium sulphate is administered.

This study was conducted retrospectively at a single tertiary referral hospital and included a relatively limited number of patients; therefore, the findings primarily reflect prescribing practices within the study setting and period. The analysis was based on information documented in medical records, which limited the evaluation to variables that were consistently available. In addition, the study focused on patterns and appropriateness of magnesium sulphate utilization and did not specifically evaluate factors associated with prescribing decisions, maternal and neonatal clinical outcomes, adverse drug reactions, or the completeness

of clinical monitoring during magnesium sulphate therapy.

Future studies involving larger populations and multiple healthcare centers are recommended to provide a broader description of magnesium sulphate utilization in patients with preeclampsia. Prospective studies may also incorporate maternal and obstetric characteristics, institutional prescribing practices, clinical monitoring parameters, adverse drug reactions, and maternal and neonatal outcomes. Such studies may provide a more comprehensive understanding of magnesium sulphate utilization and its implementation in clinical practice.

5. Conclusion

Based on the drug utilization pattern study of magnesium sulphate in pregnant women with preeclampsia at Mohammad Hoesin Hospital Palembang from July 1, 2022, to June 30, 2023, the prevalence of preeclampsia among pregnant women was 77.46%. Among pregnant women with preeclampsia who received magnesium sulphate, all were classified as having preeclampsia with severe features. Most patients were aged 20–35 years (60%), were housewives (68.9%), were multiparous (55.5%) and multigravida (80%), and had a gestational age of ≥34 weeks (71.1%). Based on the selected prescribing indicators evaluated in this study, magnesium sulphate prescribing was consistent with the predefined criteria regarding indication, dosage regimen, duration of therapy, and absence of contraindications. However, a potential pharmacodynamic interaction requiring clinical monitoring was identified among patients who received concomitant nifedipine. These findings should be interpreted within the scope of the prescribing indicators assessed and do not constitute a comprehensive evaluation of

magnesium sulphate utilization or associated clinical outcomes.

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